Appln No.: 10/009,874
Amendment Dated: May 18, 2004
Reply to Office Action of December 18, 2003

REMARKS/ARGUMENTS

This is in response to the Official Action mailed 12/18/2003. Reconsideration of the application, as amended, in view of the remarks herein is respectfully requested.

An extension of time sufficient to make this paper timely is requested, and the fee is enclosed. The Commissioner is authorized to charge any additional fees or credit any overpayment to Deposit Account No. 15-0610.

The Examiner has maintained the restriction requirement, and has therefore considered only claims 1-4, 7-24 and 46-47 in the Office Action. The non-elected claims have been canceled without prejudice in view of the decision on petition mailed March 19, 2004

Claims 46 and 47 were objected to because of dependence on non-elected claims. These claims have now been amended to overcome this objection. It is noted that no rejection on the merits was applied to these claims or to independent claims 22 or 23. Thus these claims are not further addressed in this response, and are believed to be in form for allowance.

Claims 1 and 2 stand rejected under 35 USC § 102(b) as anticipated by WO 96/11947. In order for there to be anticipation, the Examiner must show that a single reference teaches every element of the claimed invention, either expressly or inherently.

Claim 1 recites "a composition comprising at least 1 microgram of a purified nondenatured gp35 protein, with the proviso that said composition is not a gel." Claim 2 is directed to a the purified protein per se. The Examiner has not pointed to specific teachings in the reference for the various limitations in the claim, namely that the protein is "nondenatured," that the quantity of protein obtained is at least one-microgram, and that the protein is not in a gel. Thus, the Examiner has failed to show that the reference in fact meets the limitations of the claim.

It is noted that the parts of WO 96/11947 that the Examiner refers to are the claims portion of this publication. These claims, however, cannot be considered in isolation from the rest of the document since they may, as a matter of law, encompass more than is specifically disclosed. It is the specific teachings, not the generic claim language, that must be considered. Thus, the Examiner has failed to establish that there is a basis for the claim of anticipation, because no specific teaching of an isolated protein in accordance with the invention has been identified. Specific statements of the reasons for the rejection should be provided **in a non-final** official action.

It is further noted that the Examiner has stated that the absence of specific sequence the compositions of the cited reference meet the limitations of being a gp35 protein as presently claimed. Dependent claims 49 and 50 have been added to recite the sequence of Seq. ID No. 2. Thus, this distinction argued by the Examiner would not be applicable to these claims.

Claims 1-4, 7-21 and 24 stand rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

Applicants would point out, as a first matter, that the art already discusses making derivatives of gp35 of the type presently claimed. For example, the Goldberg reference cited by the examiner with respect to claims 1 and 2 discusses the same types of modifications. However, Goldberg relies on the published sequence for gp35, which is different from Seq. ID No. 2, and which in particular lacks the amino terminal amino acids of the recited sequence.

Furthermore, Applicants have very specifically set forth the genus consistent with the scope of their claims, and thus have identified their invention. The invention lies in proteins, having the correct sequence, into which conservative substitutions have been made, which retain at least one function of the native gp35 protein. As stated in the application, "conservative substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid." Thus, the physical structure of proteins within the scope of the invention is readily apparent. The Examiner's statement that the application conveys "no distinguishing information about the identity of the claimed gp35 protein variants" is therefore in error.

It is also noted that while the Examiner has cited the Patent Office Written Description Guidelines, he has not followed them. For example, in the Decision Tree for Original claims, the first step is for the Examiner to assess the features of the claimed invention that are essential to the operation/function of the claimed invention. As reflected in the specification, "the inventor has discovered that the prior art predicted amino acid sequence of gp35 lacks 77 amino acid residues at the N-terminus of the actual protein and that 15 of the 16 amino acid residues corresponding to the N-terminal residues of the prior art predicted gp35 are incorrect." These 93 initial amino acids, are important to the operation/function of the claimed invention. Indeed, specific species embodiments include fragments that consists of the amino acid sequence depicted in Figure 2 (SEQ ID NO: 2) from amino acids numbers 1-17,1-56,1-78,1-93, 8-17, 57-93, 57-64, 66- 79 or 81-93. Claim 18 refers to these fragments

plus additional possible amino acids but the limiting case is these fragments, all of which are species disclosed in the application.

Furthermore, with respect to the genus claims, the Guidelines say that "all distinguishing identifying characteristics" must be considered. Examples of such characteristics include

(a) partial structure – the basic sequence which can be modified in the variants of the invention is disclosed. The modifications are "conservative," and the meaning of this term is set forth in the application.

(b) physical and chemical properties – at least in some of the claims it is stated that the physical structure is one that retains anti-gp35 binding affinity, and the method of making anti-gp35 is disclosed.

(c) functional characteristics – a desired functional characteristic is that the amino end of the molecule retains the binding properties of gp35 which interact with P34.

(d) known or disclosed correlation between structure and function – In section 5.5.2, there is a disclosure of structure function relationships which is applicable depending on the nature of the fragment being considered. In addition, it is known that the amino end of the gp35 interacts with gp34, while the carboxy end interacts with gp36.

(e) methods for making the various structures are disclosed. Given a known DNA sequence and a known peptide sequence, it is within the skill in the art to make conservative substitutions using recombinant technology as described by making small alterations in the coding DNA sequence.

The Examiner has failed to analyze these factors in assessing compliance with the written description requirement. Thus, the written description rejection is in error and should be withdrawn.

The Examiner also rejected claims 1-4, 7-21 and 24 as lacking enablement beyond the specific protein of sequence ID No. 2. The Examiner does not challenge the teaching with respect to how to make variants of Seq. ID NO. 2 within the scope of the claims, but rather asserts that undue experimentation would be involved to find operable variants. Applicants respectfully disagree.

As a first matter, it is noted that the rejection for lack of enablement treats all claims equally. This is not appropriate. Second, the lack of guidance that the Examiner asserts is not consistent with the application. For example, the application does provide an indication of the

size of the fragments, and of areas that are suitably deleted. Thus, the application states that

> In specific embodiments, such fragments are not larger than 75,100 or 150 amino acids. In other specific embodiments, such fragments lack amino acid number 93 to 372 in Figure 2. Derivatives or analogs of gp35 include, but are not limited to, those molecules comprising regions that are substantially homologous to gp35 or fragments thereof (e.g., in various embodiments, at least 60% or 70% or 80% or 90% or 95% identity over an amino acid sequence of identical size or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art).

It is also important to note that this invention is not considered in a vacuum. Characterizations of other domains of the gp35 have already been made. For example, it is observed in the background section of the present application that it is known that "The N-terminus of P36 then attaches to the carboxy terminal region of a gp35 monomer; this interaction stabilizes P36 and forms the flexible angle joint of the tail fiber. The amino terminal region of gp35 then attaches to the C-terminus of P34 (the homooligomerization of which requires the chaperon protein gp57)." Thus the importance of the N-terminus and the C-terminus in the assembly process is known. Furthermore, the cited Goldberg reference discusses other aspects of modification of gp35 in the carboxy terminus and central portions. The sweeping statements concerning unpredictability are therefore misplaced.

Applicants agree that there are almost certainly combinations of the modifications in the central portion of the gp35 protein that would create folding patterns which would result in the burial of the N-terminal binding portion of gp35 proteins of the invention. This same can be said of any protein, however, or indeed of any claim couched in "comprising" language. It is unreasonable to expect an Applicant to test numerous composition, to provide persons skilled in the art with guidance for avoiding mistakes. Rather, applicants need to provide guidance as to how to exploit their invention. In this case, the invention is focused on the amino terminus, and ample explanation has been provided as to the portions of the amino terminus to be retained, and the types of modifications, i.e., conservative substitutions that are most appropriate. Thus, Applicants submit that the claims are enabled.

In addition to the foregoing arguments, Applicant has added claims 51-65 to define the invention in an alternative format. These claims are supported throughout the specification. The focus of these claims, however, is on the amino-terminal portion of the protein which is the part that Applicant has newly discovered and characterized.

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For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,

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